Remodulin Information for patients with Pulmonary Arterial Hypertension

Being diagnosed with Pulmonary Arterial Hypertension (PAH) can be a frightening and overwhelming experience. In the early days there can be a vast amount of information for you to understand about your illness and about the therapies your doctor has prescribed for you. The following information has been developed to offer you a comprehensive overview of PAH, to explain how Remodulin therapy can help, and to offer you the possibility to understand how best to become an active participant in your future care

Content

- An overview of Pulmonary Arterial Hypertension (PAH)
    - Your lungs and how PAH effects them
    - A detailed look at the blood vessels in the lungs
- Signs & Symptoms of PAH
    - Early stage
    - Late stage
- New York Heart Association (NYHA) Functional Classification of PAH
- Identifying the most common cause of PAH
- What is prostacyclin and how does it work
- Practical aspects of prostacyclin therapy
    - Subcutaneous infusion method
    - Where to place your infusion
    - European pump options
- The features of Remodulin
- The considerations of Remodulin
- Methods to help manage infusion site reaction and pain

An overview of Pulmonary Arterial Hypertension (PAH)

Pulmonary Arterial Hypertension (PAH) is a type of high blood pressure that develops inside the blood vessels that lead from the heart to the lungs and also those blood vessels within the lungs themselves.

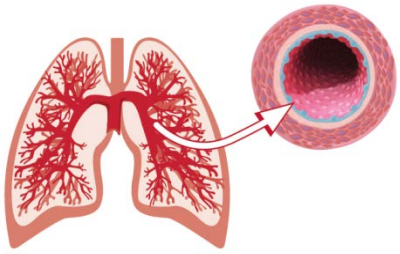
This high blood pressure is caused by an increase in the number of cells being made inside the walls of the blood vessels of the lung as well as the development of inflammation of the vessel itself.

In people who have PAH, these changes cause a gradual narrowing of the blood vessels which makes it harder for the heart to pump the right amount of blood to the lungs so as to pick up oxygen and carry it to the rest of the body.

Over time, this constant high pressure causes damage to the heart and lungs.

Your lungs and how PAH effects them

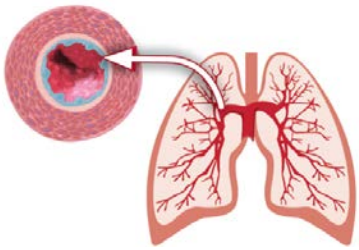
Healthy Vessel



This diagram shows the lungs and blood vessels of a healthy person

The inside of the healthy vessel is wide enough for the blood to flow freely allowing it to collect oxygen from the lungs to be taken to the rest of the body

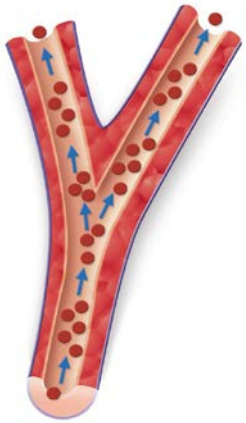
Severely Affected Vessel



This diagram shows the lungs and blood vessels of a person with PAH

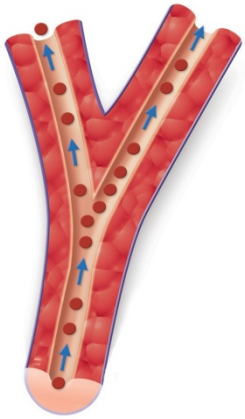
The inside of the vessels has been severely affected and narrowed by an increase of cells and inflammation. This makes it much more difficult for the blood to collect oxygen and flow through to the rest of the body

A detailed look at the blood vessels of the lungs



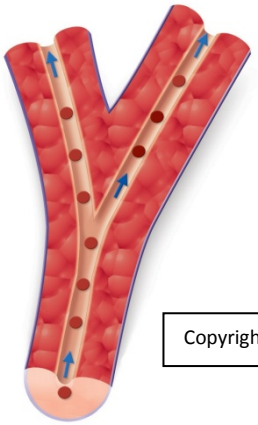
Healthy Vessel

The blood (●) which is carrying oxygen is flowing normally through the vessels to the rest of the body



Early Stage Affected Vessel

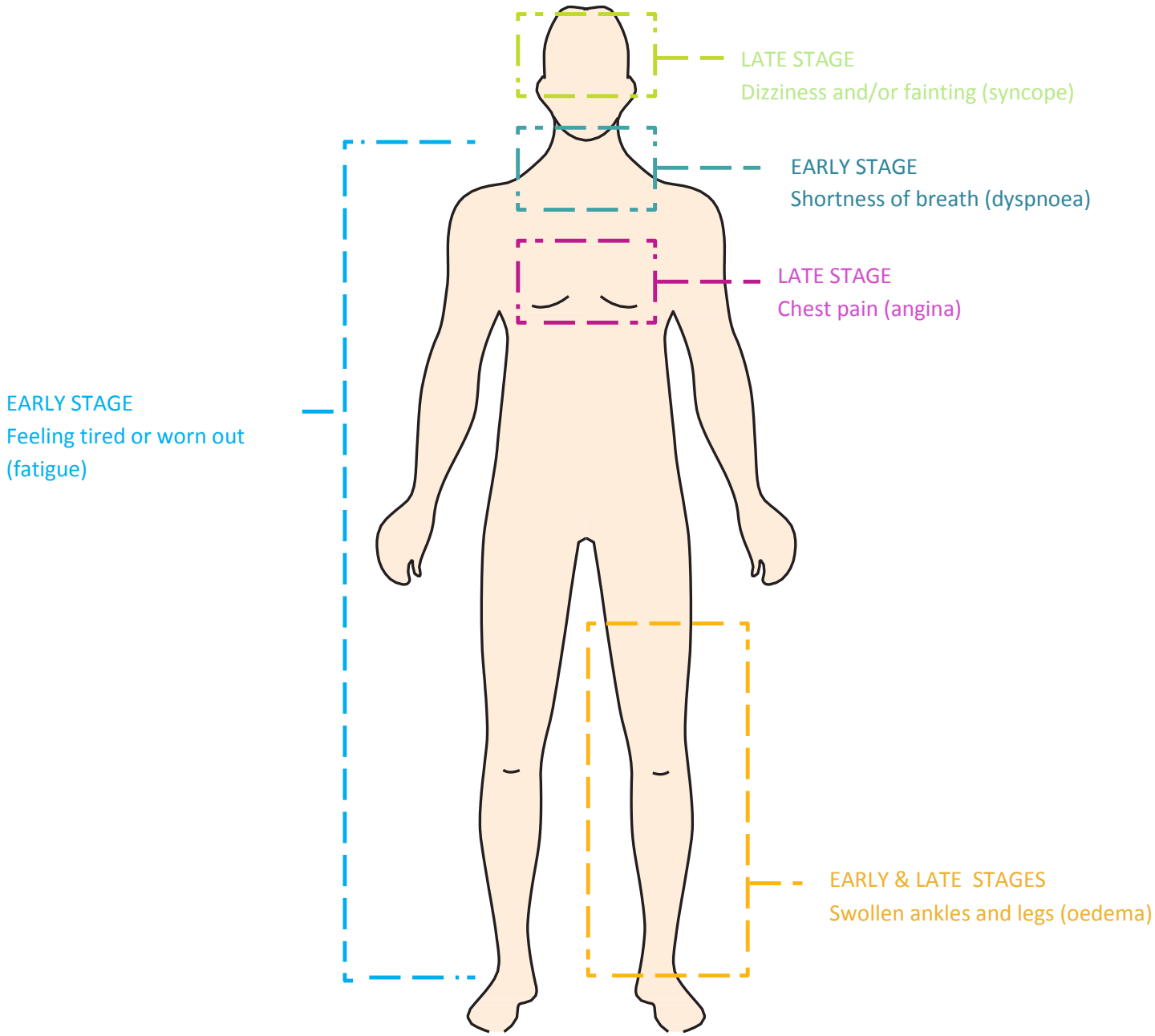
The vessel wall has some thickening caused by increased cell production and inflammation. The blood flow (●) is restricted and less oxygen is getting to the rest of the body



Late Stage Severely Affected Vessel

The vessel wall has severe thickening and inflammation. The blood flow (●) is very restricted and less oxygen is getting to the rest of the body

Signs and Symptoms of PAH - Early & Late stages

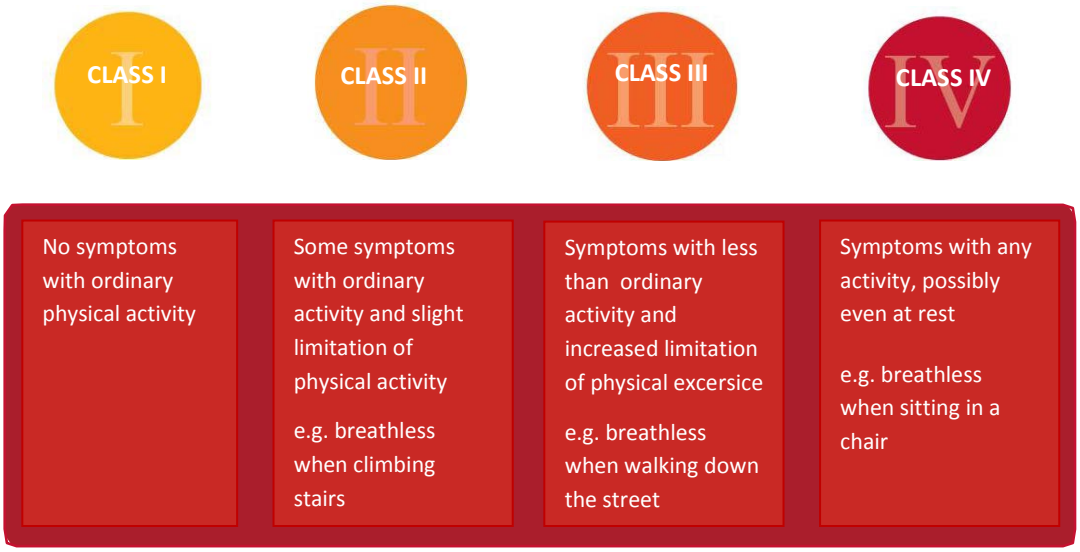


New York Heart Association (NYHA) Functional Classification of PAH

The New York Heart Association (NYHA) functional classification (FC) table was originally developed to assess the physical limitations of patients with heart disease.

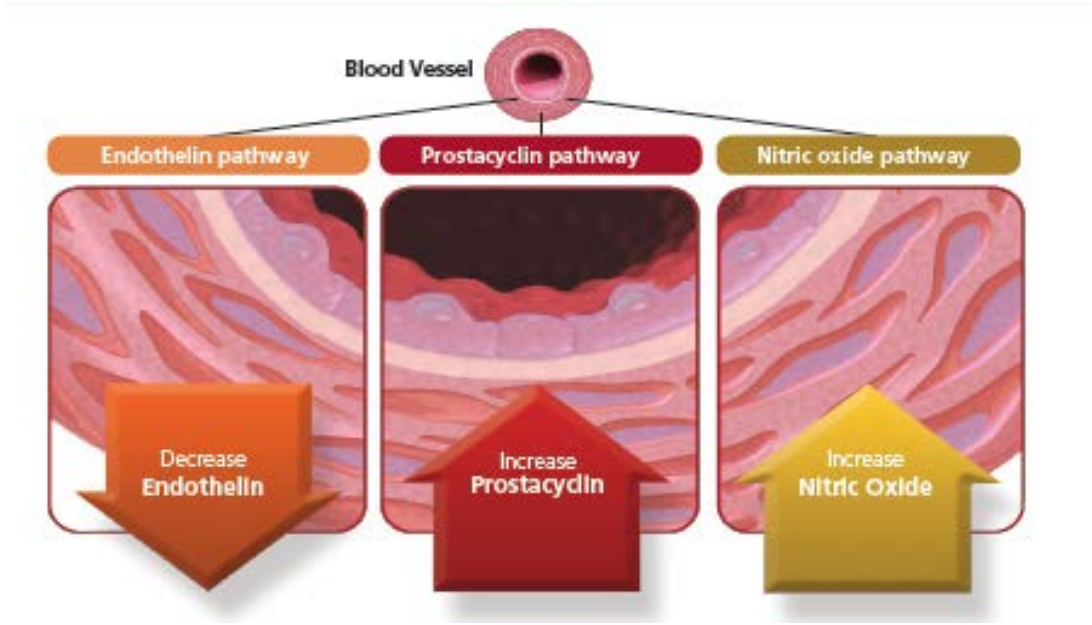
Following several revisions, the NYHA FC table is now widely used during clinical diagnosis to reflect disease severity of patients with PAH.

NYHA classification table



Another table developed by the World Heath Organisation (WHO) assists with the clinical classification of Pulmonary Hypertension (PH). There are currently 5 groups or classifications of PH. PAH is classified as WHO Group 1

The PAH pathways



The body needs the correct levels of several chemicals to keep blood vessels in the lungs working correctly

Nitric oxide, endothelin and prostacyclin are three of these chemicals that are normally present within the body and which help regulate the way in which the blood vessels work. They help by narrowing and widening the blood vessels when needed

In patients with PAH there is an imbalance of one or more of these three chemicals. For example the body may make too much endothelin and/ or too little nitric oxide or prostacyclin

When an imbalance occurs there can be too much of the chemicals that cause vessel narrowing, and too little of the chemicals that cause the blood vessels to widen in the lungs. Over time vessels become too narrow causing vessel injury and PAH to develop

What is prostacyclin and how does it work

Prostacyclin

When treating PAH there are several possible treatment pathways to choose.

Prostacyclin therapy is just one possible treatment pathway, however your

physician may choose to target one, two or more pathways at once

- Prostacyclin is a hormone that occurs naturally in our bodies. In healthy individuals it ensures our blood vessels are working properly and helps by keeping the vessels open wide

- Remodulin is an analogue (man-made version) of prostacyclin. It is manufactured to work in the same way as the body's naturally occurring prostacyclin. In PAH, prostacyclin levels are low and so Remodulin can be used as a replacement, helping to widen the blood vessels in the same way as the naturally occurring prostacyclin would normally do

- Prostacyclin analogues were amongst the first type of drugs to be discovered for the treatment of PAH and continue to be an important therapy option

- Most prostacyclin therapies need to be delivered on a continual basis via an infusion whereby the medicine enters your body under the skin or directly into a vein

How does it work?

Remodulin works in several ways:

Firstly it will help to open up the narrowed blood vessels, this will assist in improving the flow of blood, particularly to your lungs

Remodulin can also reduce the blood pressure within the vessels that lead from your heart to your lungs (pulmonary arteries), this will help to reduce the amount of work your heart has to undertake and in turn help it to function more efficiently

Together these actions can help to increase the levels of oxygen in the blood leaving your lungs that you need. This can lead to an improvement in some of the symptoms experienced with PAH such as breathlessness or fainting. It can also improve your ability to exercise on a daily basis

Practical aspects of prostacyclin therapy

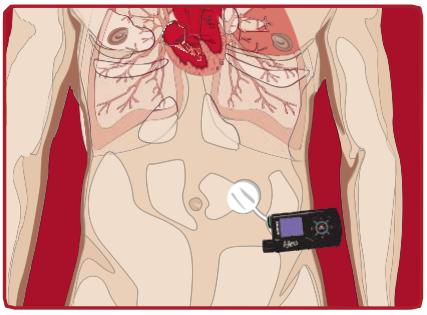
Subcutaneous (SC) infusion method

A “SC” infusion is the most common way in which Remodulin therapy is delivered into the body.

The infusion is given through the skin via a small cannula or tube. The tubing is held in place by a sticky dressing

The speed of the infusion is controlled by a miniature portable pump (about half the size of a mobile phone). The pump runs quietly and continuously in the background 24 hours a day. Remodulin is stored in a 3 ml syringe inside the pump. The Remodulin syringe needs to be changed every 3 days

Remodulin therapy can be given for a long period of time, sometimes years, so it is important to be able to care properly for your infusion system. Your Health Care Provider will help you with this and ensure that you are fully trained



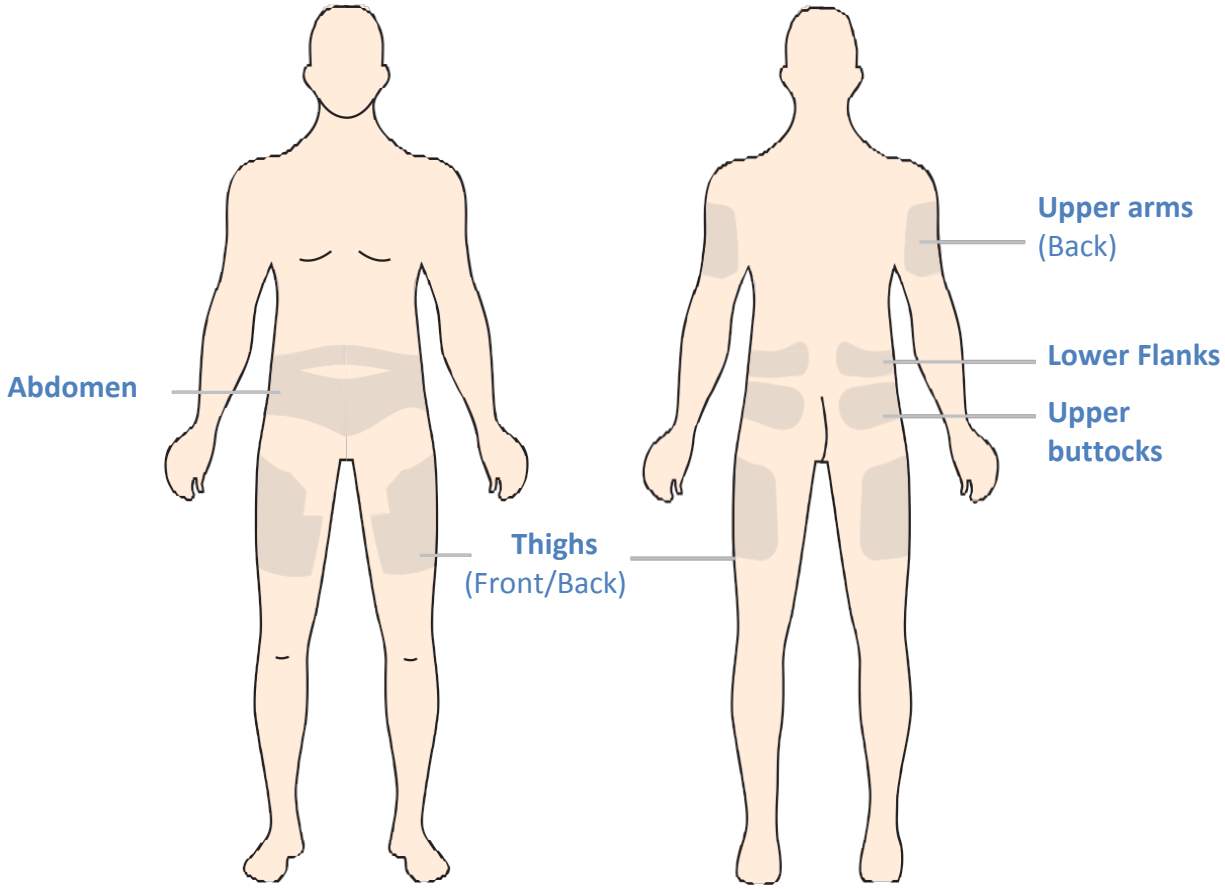
Subcutaneous Remodulin is delivered through a small catheter under the skin, generally in the abdomen area

Where to place your infusion

The abdomen is most commonly used as it is easy to see and is often the largest and therefore simplest area to access

Other possible areas to use are:

- The backs of the upper arms
- The thighs
- The rear of the hips



European infusion pump options

Here are some of the most popular pumps used in Europe. Please check with your HCP for availability in your country.

Please refer to specific pump manuals for full working instructions

Smith Medical CADD-MS® 3

Microinfusion pump

Canè Crono five

Expanded reservoir miniature pump

TwoBiens i-jet

Microinfusion pump

The features of Remodulin

Miniature Pump Options

Remodulin can be used with a variety of pumps. Your HCP will advise you about which pump is available for you

Infrequent Drug Reservoir Changes

Patients receiving SC Remodulin can go up to 72 hours before having to change their medication syringe

Stable at Higher Temperatures

Remodulin does not need to be cooled and is unaffected by changing temperatures throughout the day

The considerations of Remodulin

Remodulin is a continuous therapy that should not be stopped unless directed by your HCP

As with all therapy infusions your ability to accept and care for your infusion system is very important. Please speak to you HCP about this

When delivering Remodulin via the SC route, pain or discomfort at the infusion site can often be a challenge. However research suggests that site pain can diminish over time and about one fifth or 20% of patients will experience little or no site pain at all

The degree and sensation of site pain can be different for each patient. However most describe the feeling as being similar to a bee sting or sunburn

It is important to understand that site pain and discomfort can be effectively managed with a good site pain management strategy

Your HCP will help by discussing and developing a management strategy which is individually tailored for your needs and which will best support you through this time. Often it can take several weeks to discover what works best for you. Discuss this stage openly with your HCP, they are there to help you

Methods to help manage infusion site reaction and pain

- Published data suggests that site reaction and site pain is often at its worst 3-5 days following an infusion site change, before it begins to ease again

  Leaving the infusion site in the same position for long periods of time can help with this. Changing sites on a monthly basis can reduce the number of times you experience this discomfort. One fifth of Remodulin patients feel no discomfort at all

- Everyone has individual likes and dislikes and some infusion sites are more comfortable than others. Make a note of your good sites or bad sites. The abdomen is most often used but the backs of the upper arms, backs of the hips and upper thighs can also be used

- The Remodulin dose is not directly related to site reaction or site pain. The same discomfort can still be experienced on a low or high dose of Remodulin. Do not feel anxious if your dose has to be increased. It is better to treat PAH with the correct amount of medication and to deal with any temporary discomfort separately

- Prescribed analgesia (pain killers) can be offered by your HCP. There are many ways pain relief can be administered. Some pain killers are swallowed whilst others are creams that can be applied to the skin. Always take any medication as prescribed by your HCP. Sometimes you many need more (or less) pain relief in any one day, this can often be the case if you have recently performed an infusion site change

- The use of a diary can be a useful tool to help keep a record of when and where the pain occurs. It can help over time to identify patterns of pain and solutions to alleviate it

- Your HCP will provide you with invaluable support and guidance during your therapy. They will also provide you with close clinical follow up. Your HCP is very experienced in looking after patients just like you

- You are not alone. There are many other patients using Remodulin therapy and you may find it helpful to speak with them to learn of their experiences and challenges. The use of PH associations can be of great help.